

**REMARKS**

Claims 1 and 3-11 are presently pending in this application, as presented in the previous Response to the non-final Official Action dated March 11, 2009. Claim 2 was previously canceled without prejudice to or disclaimer of the subject matter contained therein. No claim amendment is introduced in this Response.

In view of the following remarks, further and favorable consideration is respectfully requested.

- I. At page 2 of the Official Action, claims 1 and 3-11 have been rejected under 35 USC § 103(a) as being unpatentable over Chono et al. (EP 1 201 232) in view of Hirano et al. (US Patent Application Publication No. 2002/0102290) and in further view of Terahara et al. (CA2428181).***

The Examiner asserts that it would have been obvious to modify the cited references to arrive at the presently claimed subject matter. In particular, the Examiner asserts that Chono et al. describes the use of acrylic polymers comprising at least two monomers, e.g., 2-ethylhexyl acrylate and vinyl acetate, which according to the Examiner's assertion is considered as having self-adhesion properties as well as being substantially free of carboxyl and hydroxyl groups and thus fall within the scope of the presently pending claims. The Examiner further asserts that it would have been obvious to modify the adhesive pharmaceutical preparations described in Chono et al. in view of Hirano et al. as the reference describes the weight ratio of the acrylic polymer to rubber polymer 1:2 in Example 1, and further in view of Terahara et al. as the reference describes a formulation having pergolide mesilate, an acrylic polymer, a rubber and a basic nitrogen-including polymer, to arrive at the presently claimed subject matter.

Applicants respectfully traverse this rejection. The cited references do not establish a *prima facie* case of obviousness against the presently pending claims, and any alleged *prima facie* case of obviousness is rebutted by the unexpectedly superior results of the present claims.

To establish a *prima facie* case of obviousness, the PTO must satisfy three requirements. First, as the U.S. Supreme Court held in *KSR International Co. v. Teleflex Inc. et al.*, 550 U.S. 398 (2007), "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." See *KSR International Co. v. Teleflex Inc. et al.*, 550 U.S. 398 at 417-418. Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior

art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

Further, a *prima facie* case of obviousness, if established, can be rebutted when the claimed invention yields unexpectedly improved properties or properties not present in the prior art. Rebuttal evidence may consist of a showing that the claimed compound possesses unexpected properties. *In re Dillon*, 919 F.2d at 692-93, 16 USPQ2d at 1901. When considering whether proffered evidence is commensurate in scope with the claimed invention, office personnel should not require the applicants to show unexpected results over the entire range of properties possessed by a chemical compound or composition. *In re Chupp*, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987). Evidence that the compound or composition possesses superior and unexpected properties in one of a spectrum of common properties can be sufficient to rebut a *prima facie* case of obviousness. *Id.*

### ***Present Subject Matter***

The present subject matter, as described in independent claim 1, is directed to a patch comprising a backing layer and an adhesive layer disposed on the backing layer and compounded with an adhesive base agent and pergolide and/or a pharmaceutically acceptable salt thereof, wherein the adhesive base agent comprises an acrylic polymer including **no** carboxyl group and hydroxyl group in the molecule and having self-adhesion properties, a rubber polymer, and a basic nitrogen-including polymer including a basic nitrogen and having no self-adhesion properties, wherein a weight ratio of the content of the acrylic polymer to the content

of the rubber polymer is from 1:1 to 1:9, and wherein a weight ratio of the total content of the acrylic polymer and the rubber polymer to the content of the basic nitrogen-including polymer is from 9:1 to 1:1. The present subject matter shows an enhanced skin permeation rate and/or patch property superior to the prior art.

Claims 3-11 each depend, either directly or indirectly, from claim 1 and thus contain all the limitations of claim 1, as noted above.

***Chono et al.***

Chono et al. describe a patch formulation comprising a basic drug (e.g., pergolide, ondansetron), an adhesive layer, and a backing layer for supporting the adhesive layer. Chono et al. describe, at paragraph [0030], that the adhesive layer may contain a lipophilic/hydrophobic polymer including SIS or PIB (rubber) and an acrylic polymer that is a copolymer of at least two monomers selected from the group consisting of 2-ethylhexyl acrylate, vinyl acetate, methacrylates, methoxyethyl acrylate and acrylic acid.

However, Chono et al. ***does not expressly teach*** a specific acrylic polymer having no carboxylic or hydroxyl group in the molecule, much less the combined use of an acrylic polymer having no carboxylic or hydroxyl group in the molecule with a rubber polymer disclosed therein. Although Chono et al. describe in one line that the hydrophobic polymers may be used alone or in combination, see paragraph [0031], there is no concrete teaching or suggestion. See the first sentence in each of paragraphs [0016], [0018], [0021], [0027], [0029], [0031], [0033] etc. ***Nowhere*** Chono et al. specifically describe a combined use of an acrylic polymer with a rubber

polymer. Chono et al. provide no specific compositions or examples for the combined use, as well as no specific acrylic polymer having no carboxyl and hydroxyl groups. All of the examples of Chono et al. teach the combined use of rubber polymers, PIB and SIS only.

In addition, as the Examiner concedes in the Official Action Chono et al. do not disclose a “basic nitrogen-including polymer that includes a basic nitrogen and having no self-adhesion property,” as required by the present subject matter.

Accordingly, Chono et al. fail to teach or suggest all the elements of the presently claimed subject matter. Also, Chono et al. do not provide any teaching or suggestion of the combined use of an acrylic polymer having no carboxylic and hydroxyl groups with a rubber polymer disclosed therein.

***Hirano et al.***

Hirano et al. describe a percutaneous therapeutic apparatus having at least three (3) layers comprising a medicine non-permeable backing layer, a medicine storage layer containing serotonin-receptor antagonist between said backing layer and medicine-releasing layer, and a pressure-sensitive adhesive layer which is able to control release of medicine. See page 11 of Hirano et al. In Example 1, Hirano et al. further describe a combination of a rubber polymer (SIS) with 2-ethylhexyl acrylate/vinyl acetate copolymer for a serotonin receptor antagonist.

However, ***nowhere*** Hirano et al. teach or suggest the active ingredient “pergolide” or a “basic nitrogen-including polymer that includes a basic nitrogen and having no self-adhesion property,” as required by the presently claimed subject

matter.

Accordingly, not only does Hirano et al. fail to teach or suggest all the elements of the present subject matter, but also Hirano et al. provide no teaching or suggestion of the combined use of an acrylic polymer and a rubber polymer disclosed therein, for the active ingredient "pergolide."

***Terahara et al.***

Terahara et al. describe a transdermal preparation containing a polymer compound having amino groups, a drug forming an acid addition salt, and carboxylic acid and/or a salt thereof, characterized in that the content of the polymer compound having amino groups is 50% or less by weight based on the whole preparation, and a molar ratio of the amino groups in the polymer compound is 0.5 mol or higher per mol of the drug, and the content of the carboxylic acid and/or the salt thereof is 1 to 10 mol per mol of the sum of the drug and the amino groups in the polymer compound. Further, Terahara et al. describe a basic nitrogen-including polymer being a methyl methacrylate-butyl methacrylate-dimethylaminoethyl methacrylate terpolymer (Brand name: Eudragit E), or polyvinyl acetal diethylamino acetate, at page 6, lines 24-25. Furthermore, Terahara et al. describe two specific examples, i.e., Example 5 and Example 6, for preparations comprising pergolide mesylate, SIS, an acrylic polymer and Eudragit E100.

However, ***nowhere*** does Terahara et al. describe a combined use of the basic nitrogen-including polymer with ***an acrylic polymer having no carboxyl and hydroxyl groups***. Even though Terahara et al. describe in Examples 5 and 6 the

combined use of the basic nitrogen-including polymer with an acrylate polymer, "Duro-Tak 387-2287," and a rubber polymer (SIS), for the active ingredient of pergolide, the acrylate polymer of "Duro-Tak 387-2287" used in the examples does **have a hydroxyl group** in the molecule, and thus is excluded from the "acrylic polymer including no carboxyl group and hydroxyl group in the molecule and having self-adhesion properties," as required by the presently claimed subject matter. In this respect, it can be said that both the examples of Terahara et al. actually **teach away** from the combined use of the basic nitrogen-including polymer and rubber polymer, with an acrylic polymer having no carboxyl and hydroxyl groups, for the active ingredient "pergolide."

As such, not only do Terahara et al. fail to teach all of the elements of the presently claimed subject matter, but also Terahara et al. provide no teaching or suggestion of the combined use of the basic nitrogen-including polymer with an acrylic polymer having no carboxyl and hydroxyl groups. Instead, the reference actually teaches away from the combined use of the basic nitrogen-including polymer with an acrylic polymer having no carboxyl and hydroxyl groups.

***A prima facie case of obviousness has not been established since there is no reason to combine the prior art elements in the same way as the present claims require.***

As discussed above, neither Chono et al., nor Hirano et al. describe the essential component of "a basic nitrogen-including polymer including a basic nitrogen and having no self adhesion property," as required by the presently claimed subject matter. Accordingly, for the use of the component in combination with two other

components, a person of ordinary skill in the art would have had to look at the teachings of Terahara et al.

In this case, Terahara et al. provide only two examples, i.e., Example 5 and Example 6, teaching the use of the basic nitrogen-including polymer with other polymers, for the active ingredient of pergolide mesilate. However, both the examples teaches a combination of the basic nitrogen-including polymer and the rubber polymer (SIS), ***with the acrylic polymer of "Duro-Tak 387-2287" which contains a hydroxyl group in the molecule.*** However, the acrylic polymer containing carboxyl and hydroxyl groups in the molecule is clearly excluded from the present claims. That is, Terahara et al. actually teaches away from the combined use of an acrylic polymer having no carboxyl and hydroxyl groups with the basic nitrogen-including polymer and the rubber polymer, for the active ingredient of pergolide or its pharmaceutically acceptable salt.

Accordingly, contrary to the Examiner's allegation in the Official Action regarding the obviousness of the combination, the person of ordinary skill would have had no reason to choose only the basic nitrogen-including polymer from the teaching of Terahara et al. and combine this component with the other two polymers, i.e., an acrylic polymer having no carboxyl and hydroxyl groups in the molecule and a rubber polymer to arrive at the present subject matter. With no ***hindsight***, there is no reason for the ordinarily skilled person to be motivated to choose and combine the prior art elements in the way the present claims require, in spite of the description of the closest preparations containing all of three components, i.e., pergolide mesylate, SIS, Eudragit E100 (a basic nitrogen-including polymer), in combination with the



acrylic polymer "Duro-Tak 387-2287" which contains a hydroxyl group in the molecule.

Furthermore, as discussed above, Chono et al. do not expressly teach an acrylic polymer having no carboxyl and hydroxyl groups; only a possible copolymer of at least two monomers selected from the group including 2-ethylhexyl acrylate and vinyl acetate, is described in Chono et al. Accordingly, the Examiner's assertion that Chono et al. disclose the use of acrylic polymer having no carboxyl and hydroxyl groups with a rubber polymer is not agreeable to Applicants. Also, as discussed above, although Hirano et al. describe the combined use of the acrylic polymer of 2-ethylhexyl acrylate/vinyl acetate with a rubber polymer, Hirano et al. do not at all describe the active ingredient, pergolide or pharmaceutically acceptable salts thereof. Applicants direct the Examiner's attention to the KSR court holding that "it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine ***whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue.*** "[I]t [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ... it can ***be important to identify a reason that would have prompted a person of ordinary skill in the relevant field***

***to combine the elements in the way the claimed new invention*** does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." [Emphasis added] See *KSR International Co. v. Teleflex Inc. et al.*, 550 U.S. 398 at 417-418.

Furthermore, Applicants note the Examiner's assertion that the Terahara et al. reference has been applied only for the disclosure of the basic nitrogen including polymer. Applicants respectfully point out that the entirety of the reference must be considered when in determining the scope and content of the reference. *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, (Fed. Cir 1983), *cert. denied*, 469 U.S. 851 (1984). The Examiner therefore must acknowledge any disclosure in the reference that teaches away from the presently pending claims. *Id.*

In view of foregoing, Applicants respectfully submit that the cited references do not establish a *prima facie* case of obviousness against the presently claimed subject matter. Reconsideration and withdrawal of the rejection of claims 1 and 3-11 under 35 USC §103(a) is therefore respectfully requested.

***Any alleged prima facie case of obviousness is rebutted by the unexpected results of the present claims***

Applicants additionally submit that the presently claimed subject matter shows unexpectedly superior results and advantages that are not presented in the prior art, which rebuts any alleged *prima facie* case of obviousness. *In re Dillon*, 919 F.2d at 692-93, 16 USPQ2d at 1901. Rebuttal evidence may include evidence that the claimed subject matter yields unexpectedly improved properties or properties not

present in the prior art. Rebuttal evidence may consist of a showing that the claimed compound possesses unexpected properties. See *In re Dillon*. Further, rebuttal evidence and arguments can be presented in the specification, *In re Soni*, 54 F.3d 746, 750, 34 USPQ2d 1684, 1687 (Fed. Cir. 1995), by counsel, *In re Chu*, 66 F.3d 292, 299, 36 USPQ2d 1089, 1094-95 (Fed. Cir. 1995), or by way of an affidavit or declaration under 37 CFR 1.132, e.g., *Soni*, 54 F.3d at 750, 34 USPQ2d at 1687; *In re Piasecki*, 745 F.2d 1468, 1474, 223 USPQ 785, 789-90 (Fed. Cir. 1984).

Applicants direct the Examiner's attention to the unexpectedly superior properties of the presently claimed subject matter described in the present specification and outlined in Tables 1-3 on pages 33-35 of the specification. The data clearly shows enhanced maximum skin permeation rates and/or patch properties for the active ingredient, pergolide in those examples that contain all the components as recited in the presently pending claims when compared to prior art examples where one or more of the claimed components are not present in the composition and reflect those described in the cited references. These effects of enhanced skin permeation and/or patch property are not presented in the prior art of record.

In particular, Applicants draw the Examiner's attention to Examples 1-3 representing the patch composition containing all of the presently claimed components and meeting the requirement of present claim 1. Contrary to the Examiner's understanding that Examples 1-6 represent the presently pending claims and there is no particularly superior effects in the permeation rate in view of the

comparative examples, only Examples 1-3 represent the patch compositions meeting all of the limitations of the presently pending claims.

Examples 4-6 represent patch compositions in which methyl methacrylate-butyl methacrylate-dimethylaminoethyl methacrylate terpolymer (Eudragit E, a basic nitrogen-including polymer including a basic nitrogen and having no self-adhesion property) is not used though a weight ratio of the acrylic polymer to the rubber polymer is within the claimed range of from 1:1 to 1:9.

Comparative Example 4 represents a patch composition in which the weight ratio of the acrylic polymer to the rubber polymer is out of the claimed scope, from 1:1 to 1:9, and methyl methacrylate-butyl methacrylate-dimethylaminoethyl methacrylate terpolymer (i.e., Eudragit E, a basic nitrogen-including polymer including a basic nitrogen and having no self-adhesion property) is not used. This patch composition corresponds to that of Chono et al.

Comparative Examples 5-7 represent patch compositions that include an acrylic polymer having a hydroxyl group (DURO-ATK87-2287). These patches correspond to those of Terahara et al.

Comparative Examples 8-10 represent patch compositions that include an acrylic polymer having a carboxyl group (DURO-ATK87-2852). These patches correspond to those of Terahara et al.

Tables 1-3 on pages 33-35 of the present specification clearly demonstrate that the present compositions of Examples 1-3 are superior to those of Example 4-6 and Comparative Examples 4-10 in skin permeability and/or patch properties. The

results support the unexpectedly superior results of the claimed subject matter as compared to the cited prior art compositions.

As such, Applicants submit that any alleged *prima facie* case of obviousness is rebutted by the unexpectedly superior results of the presently claimed subject matter. See *In re Dillon*. The Examiner is respectfully requested to reconsider and withdraw the rejection of claims 1 and 3-11 under 35 U.S.C. §103(a).

***II. At pages 10-13 of the Official Action, claims 1 and 5-8 have been provisionally rejected under the Judicially Created Doctrine of Obviousness-Type Double Patenting.***

The Official Action states that claims 1 and 5-8 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 8 and 12 of copending U.S. Patent Application No. 10/469,612 (hereinafter "the '612 Application"). The Examiner acknowledges that claims 1, 8 and 12 of the '612 Application fail to teach or suggest a weight ratio of the content of the acrylic polymer to the content of the rubber polymer being from 1:1 to 1:9, and a weight ratio of the total content of the acrylic polymer and the rubber polymer to the content of the basic nitrogen-including polymer being from 9:1 to 1:1, as presently claimed. However, the Examiner asserts that it would have been obvious to modify the weight ratios in order to arrive at the presently claimed subject matter.

Applicants respectfully request that the Examiner hold this rejection in abeyance until such time as the Examiner indicates there is successful resolution of

the claim rejections noted above. Applicants, at that time, will either address the rejection or file a terminal disclaimer over the '612 Application.

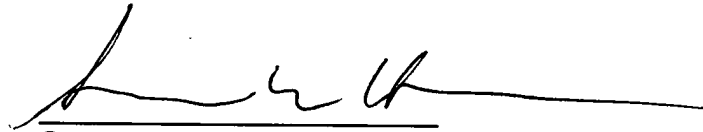
**CONCLUSION**

In view of the foregoing, Applicants submit that the application is in condition for immediate allowance. Early notice to that effect is earnestly solicited. The Examiner is invited to contact the undersigned attorney if it is believed that such contact will expedite the prosecution of the application.

In the event this paper is not timely filed, Applicants petition for an appropriate extension of time. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

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